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CONFIDENTIAL

THE EFFECTS OF CIGARETTE SMOKING ON THE HUMAN BRAIN AND CARDIOVASCULAR SYSTEM

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The cerebral effects of smoking tobacco have been described by many men. Some of these descriptions have stated that tobacco has a quieting and relaxing effect and some have stated it has a stimulating effect. However, few objective studies of these cerebral effects have been reported.

Methods

Paid subjects were chosen at random from the student population. They were young men varying in age from 17 to 24 years. Five were smokers (1 to 1½ package per day) and 2 did not smoke. A 12 hour period of abstinence from smoking was required in all cases. Studies were accomplished in the morning, with the subjects in a fasting state in the supine position.

After the introduction of the needles and the application of the electrocardiographic and electroencephalographic leads, a 30 minute rest period was observed. Following this period, control observations were made. The subject was then instructed to smoke 3 consecutive cigarettes within 30 minutes. Four-fifths of each cigarette was consumed in 8 to 10 minutes. Only one brand of a normal length cigarette was used in an attempt to keep this factor constant. After finishing the last cigarette, experimental studies were accomplished. Electrocardiograms (lead II), electroencephalograms, and intraarterial pulse pressure wave recordings were made at frequent (2 to 4 minute) intervals before, during and after smoking. Cerebral blood flows (1), arterial and cerebral blood gases (2) and pH (3) were measured before and from 1 to 10 minutes after finishing the third cigarette. Cerebral metabolism and cerebral vascular resistance were calculated as previously described (1). Arterial and cerebral venous pCO_2 were calculated by means of the nomogram of Peters and Van Slyke (2). Arterial O_2 capacity and saturation were determined (4).

Results and Discussion (See Table I)

The only changes noted were a statistically significant increase in pulse rate and a consistent change in the electroencephalographic patterns. In all 7 cases, an intermittent flattening appeared on the electroencephalographic recordings (see Figure I). This

flattening occurred only during smoking of cigarettes and lasted from 1 to 30 seconds. Even in the 2 individuals who did not inhale, this flattening occurred but was shorter in duration. Dr. Chaskiel Grossman, our electroencephalographer, thought it was impossible to determine if the flattening was caused by the cigarette or was merely an abnormal attention response.

In one of the young men, electrocardiograms revealed a biphasic T wave 1 minute after the start of the first cigarette. Four minutes later the T waves became flat. Three minutes after the third cigarette the T waves returned to normal. In another individual a sinus arrhythmia occurred. These changes have been reported by others.

There were no significant changes in cerebral blood flow, cerebral metabolism, cerebral arteriovenous oxygen difference, cerebral vascular resistance, cerebral R. Q., hemoglobin, arterial O_2 capacity, O_2 saturation, arterial and internal jugular O_2, CO_2, pH and pCO_2. The lack of significant change in mean arterial blood pressure has also been previously reported.

It is possible to attribute the lack of significant changes in cerebral hemodynamics and metabolism in this youthful group to the good condition of their cardiovascular systems. Therefore, it is thought to be of interest and importance to repeat these studies in individuals of the older age group (over 60 years). In addition, intravenous nicotine would allow the accomplishment of these studies during, instead of after, administration of the drug. The use of denicotinized cigarettes may help to determine the cause of the intermittent flattening found on the electroencephalographic records.

Summary

In 7 normal young men the effects of smoking 3 normal sized cigarettes in 30 minutes were studied. Cerebral blood flows, cerebral metabolism, blood gases, blood pH, electrocardiograms, arterial pulse pressure curves, and electroencephalograms were accomplished before, during, and after smoking. Besides a significant increase in the pulse rate and the consistent presence of intermittent flattening of the electroencephalographic recordings, no significant changes were noted. The value of repeating these studies in older people and with intravenous nicotine or denicotinized cigarettes is discussed.

References

1. Kety, S. S. and Schmidt, C. F. The Nitrous Oxide Method for the Quantitative Determination of Cerebral Blood Flow in Man; Theory, Procedure and Normal Values. J. Clin. Invest., 1948, 27, 476.

2. Peters, J. P. and Van Slyke, D. D. Quantitative Clinical Chemistry, Vol. II, Methods, Williams and Wilkins, Baltimore, 1932.

3. Rosenthal, T. B. Effect of Temperature on pH of Blood and Plasma Vitro. J. Biol. Chem., 1938, 126, 655.

4. Comroe, J. H. Jr., Methods in Medical Research, Vol. 2, p. 142, Year Book Publishers, Inc., Chicago, 1950.

Table I a

Subject	Age	Remarks	Time 3rd Cig to 2nd CBF	CBF cc/100 g/min. B	CBF cc/100 g/min. A	CMR O_2 cc O_2 100 g/ min. B	CMR O_2 cc O_2 100 g/ min. A	(A-V) O_2 Vols %^{2} B	(A-V) O_2 Vols %^{2} A	CVR mm Hg/100 g/min. B	CVR mm Hg/100 g/min. A	CRQ B	CRQ A
WY	20	Smokes about 1½ pack per day	10	94	54	5.9	3.0	6.3	5.6	0.9	1.6	1.06	1.00
CY	23	Smokes at least 1 pack/day	2	50	63	3.4	4.0	6.7	6.4	1.7	1.5	1.06	1.00
JB	19	Smokes at least 1 pack/day	6	52	61	3.7	4.4	7.2	7.2	1.5	1.4	0.97	0.97
JH	20	Used to smoke. Not for 2 yrs Did not inhale	8	72	40	3.9	3.2	5.5	8.1	1.2	2.2	1.00	1.00
MR	17	Smokes 1½ pack/day	1	72	72	3.8	3.9	5.3	5.4	1.2	1.2	1.00	1.02
MM	23	Non-smoker Did not inhale	3	47	45	3.1	3.3	6.5	7.4	1.8	1.8	1.01	1.07
RS	24	Smokes 1 pack/day	4	55	47	3.9	4.0	7.0	8.6	1.5	1.7	1.01	.89
Mean				63	55	4.0	3.7	6.4	7.0	1.4	1.6	1.02	.99
SE				6.4	4.3	0.3	0.2	0.3	0.4	0.1	0.1	0.01	0.02

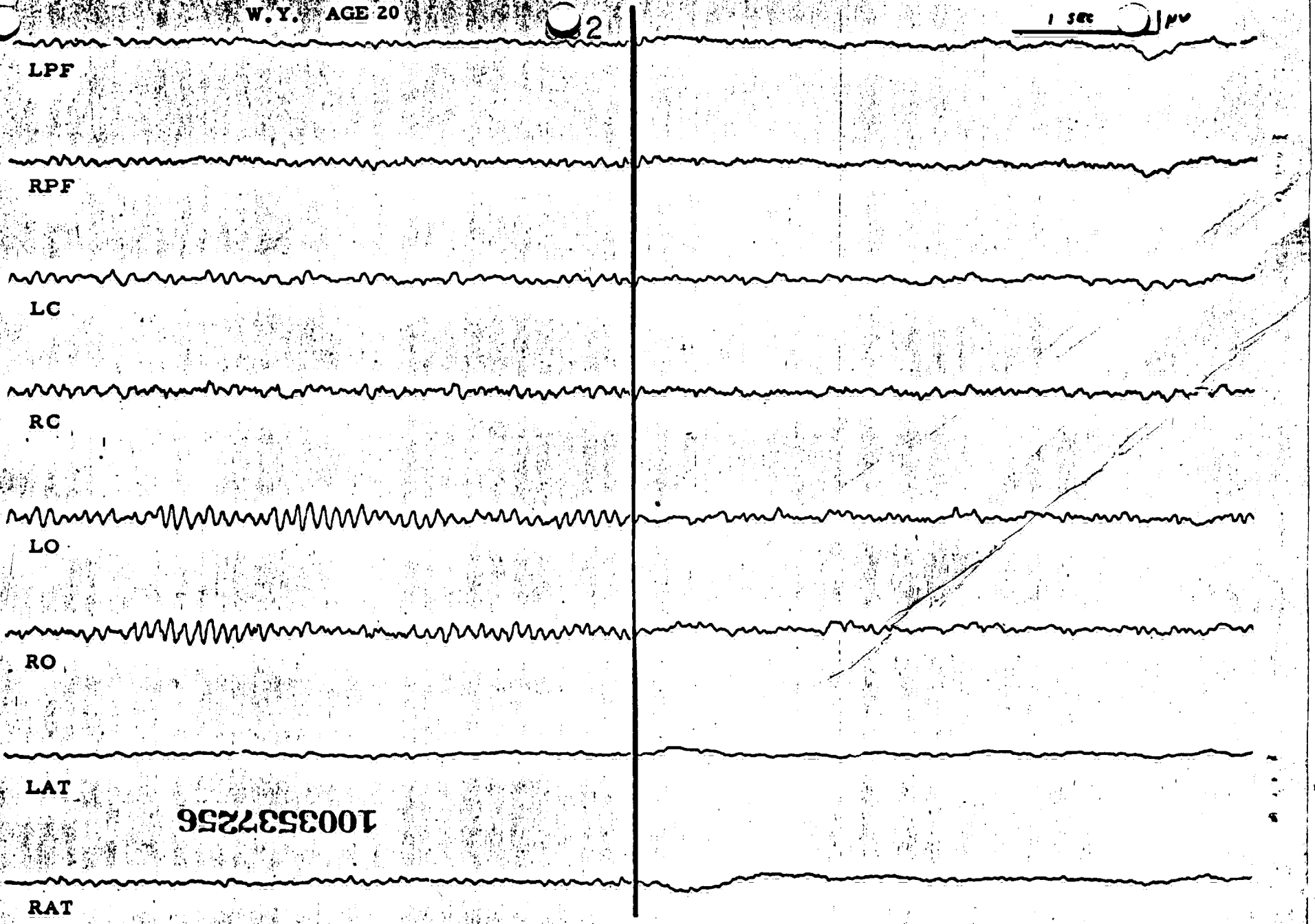
Key - CBF--Cerebral Blood Flow
CMR O_2--Cerebral Metabolic Rate (oxygen consumption
A--After Smoking
B--Before Smoking
CVR--Cerebral Vascular Resistance
CRQ--Cerebral Respiratory Quotient
SE--Standard Error

Table I b

Subject	O_2 Content Vols. % Arterial B	O_2 Content Vols. % Arterial A	O_2 Content Vols. % Venous B	O_2 Content Vols. % Venous A	O_2 Cap. Vols.% B	O_2 Cap. Vols.% A	O_2 Sat. % B	O_2 Sat. % A	Pulse/min. B	Pulse/min. A	MABP mm. Hg. B	MABP mm. Hg. A	Hb. gms/100 cc B	Hb. gms/100 cc A	CO_2 Content Vols.% Arterial B	CO_2 Content Vols.% Arterial A	CO_2 Content Vols.% Venous B	CO_2 Content Vols.% Venous A
BY	19.8	18.3	13.5	12.7	20.1	18.6	100	100	80	80	81	85	14.9	14.9	45.9	46.4	52.6	52.0
CY	19.2	19.7	12.5	13.3	20.5	21.4	95	93	60	75	83	95	15.4	15.9	46.5	47.8	53.6	54.2
JB	19.5	19.5	12.3	12.3	20.5	20.6	97	96	72	80	80	85	15.1	15.1	45.5	45.5	52.5	52.5
JH	19.5	19.7	14.0	11.6	21.5	20.9	92	95	84	96	88	87	15.3	15.3	47.6	44.9	53.1	53.0
MR	17.9	18.2	12.6	12.6	19.0	19.7	96	94	74	90	91	88	14.5	14.9	49.2	49.2	54.5	54.7
MM	19.0	19.4	12.4	12.0	20.4	20.7	95	95	68	77	84	82	16.0	16.0	47.5	45.7	54.0	53.6
RS	19.0	18.6	12.0	10.0	20.0	19.7	96	96	60	76	81	81	14.5	14.4	45.6	43.2	52.7	50.8
Mean	19.1	18.9	12.8	12.1	20.3	20.2	96	96	71	82	84	86	15.1	15.2	46.8	46.1	53.3	53.0
SE	0.2	0.3	0.2	0.4	0.3	0.3	1	1	3.4	3.0	1.5	1.7	0.2	0.2	0.5	0.7	0.3	0.5

Table I c

Subject	pH Arterial B	pH Arterial A	pH Venous B	pH Venous A	C.V.I. B	pCO_2 mm Hg A	pCO_2 mm Hg B	pCO_2 mm Hg A	EEG
BY	-	-	-	-	-	-	-	-	Intermittent flattening lasts 4 to 30 seconds, flattening duration decreased as smoking continued. Started 3 minutes after first cigarette started. Flattening stopped within 3 to 12 seconds after cigarette.
CY	7.40	7.41	7.36	7.37	40	40	50	50	Intermittent flattening lasts 3 to 15 seconds. Started 25 seconds after first cigarette started. Flattening continued for 10 minutes after last cigarette.
JB	7.42	7.42	7.38	7.38	38	38	48	48	Intermittent flattening lasts 5 to 10 seconds. Started 1 min. after starting first cigarette. Flattening stopped within 30 seconds of last cigarette.
JH	7.38	7.41	7.31	7.35	43	38	56	51	Intermittent flattening lasts 1 to 3 seconds, starting 4 minutes after starting first cigarette. No inhaling.
MR	7.42	7.40	7.37	7.37	40	42	50	50	Intermittent flattening lasts 5 seconds. Started over a minute after start of first cigarette. 8/second alpha control and 9/second during smoking.
MM	7.41	7.41	7.35	7.37	40	38	52	49	Two seconds of flattening after start of first cigarette. Seven second flattening at end of first cigarette. During second cigarette 4 second intermittent flattening. None without cigarette. Intermittent flattening during third cigarette. Decreased amplitude of alpha waves.
RS	7.42	7.43	7.41	7.39	38	35	44	42	Intermittent flattening lasts 2 to 6 seconds.
Mean	7.41	7.41	7.36	7.37	40	39	50	48	
SE	0.01	0.01	0.01	0.01	0.7	0.9	1.5	1.2	



EFFECT OF CIGARETTE SMOKING ON ELECTROENCEPHALOGRAPHIC PATTERN